Molnupiravir Capsules

Molnupiravir Capsules contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of molnupiravir, $C_{13}H_{19}N_3O_7$.

Usual strengths. 200 mg; 400 mg.

Identification

In the Assay, the principal peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with reference solution (a).

Tests

Dissolution (2.5.2).
Apparatus No. 2 (Paddle),
Medium. 500 ml of *0.1 M hydrochloric acid,*
Speed and time. 50 rpm and 30 minutes.

Withdraw a suitable volume of the medium and filter.

Determine by liquid chromatography (2.4.14).

Solvent mixture. 90 volumes of a 0.154 per cent w/v solution of *ammonium acetate* in *water,* adjusted to pH 4.75 with *glacial acetic acid* and 10 volumes of *methanol.*

Test solution. Use the filtrate, dilute if necessary, with the dissolution medium.

Reference solution. A 0.04 per cent w/v solution of *molnupiravir IPRS* in the solvent mixture.

Chromatographic system
- a stainless steel column 5 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (3.5µm) (Such as Xselect CSH, C18), and a guard column 1 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (3 µm),
- sample temperature: 5º,
- mobile phase A: a 0.1 per cent v/v solution of *orthophosphoric acid* in *water,*
  B: *methanol,*
- a gradient programme using the conditions given below,
- flow rate: 1 ml per minute,
- spectrophotometer set at 260 nm,
- injection volume: 5 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	95	5
3	40	60
3.1	95	5
6	95	5

Inject the reference solution. The test is not valid unless the column efficiency is not less than 10000 theoretical plates, the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 2.0 per cent.

Inject the reference solution and the test solution.

Calculate the content of $C_{13}H_{19}N_3O_7$ in the medium.

Q. Not less than 80 per cent of the stated amount of $C_{13}H_{19}N_3O_7$.

Related substances. Determine by liquid chromatography (2.4.14).

Solvent mixture. 90 volumes of 0.154 per cent w/v solution of *ammonium acetate* in *water,* adjusted to pH 4.75 with *glacial acetic acid* and 10 volumes of *methanol.*

Test solution. Disperse a quantity of the mixed content of capsules containing 1.0 g of Molnupiravir in 100 ml of the solvent mixture, with the aid of mechanical shaker for 60 minutes and dilute to 250.0 ml with the solvent mixture. Centrifuge a portion of the solution at 4000 rpm for 10 minutes. Dilute 5.0 ml of the supernatant to 50.0 ml with the solvent mixture.

Reference solution (a). A 0.04 per cent w/v solution of *molnupiravir IPRS* in the solvent mixture.

Reference solution (b). Dilute 1.0 ml of reference solution (a) to 100.0 ml with the solvent mixture.

Reference solution (c). Transfer 80 mg of *molnupiravir IPRS* to a 200-ml volumetric flask, add 10 ml of *1 M hydrochloride acid* and mix. Keep on heating in water-bath at 50º for 15 minutes. Then neutralize with equal volume of *1 M sodium hydroxide*, mix and dilute to volume with the solvent mixture.

Chromatographic system

– a stainless steel column 15 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (2.5 µm) (Such as Waters Xselect CSH, C18), and a guard column 1 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (3 µm),

– column temperature: 45º,

– mobile phase: A. a mixture of 98 volumes of 0.1 per cent v/v solution of *formic acid* in *water* and 2 volumes of *acetonitrile,*

B. *acetonitrile,*

– a gradient programme using the conditions given below,

– flow rate: 1 ml per minute,

– spectrophotometer set at 260 nm,

– injection volume: 5 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	100	0
18	20	80
20	100	0
26	100	0

Name	Relative retention time	Correction factor
N-hydroxycytidine[1]	0.38	0.72
Molnupiravir impurity A* (unknown structure)	0.49	--
Molnupiravir	1.0	--
Molnupiravir impurity B* (unknown structure)	1.04	--

*Impurities shall be reported under any unspecified impurities.

[1]1-((2R,3R,4S,5R)-3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-4-(hydroxyamino)pyrimidin-2(1H)-one.

Inject reference solution (b) and (c). The test is not valid unless the resolution between the peaks due to molnupiravir and molnupiravir impurity B is not less than 1.5 in the chromatogram obtained with reference solution (c), the column efficiency is not less than 10000 theoretical plates, the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 5.0 per cent in the chromatogram obtained with reference solution (b).

Inject reference solution (b) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to N-hydroxycytidine is not more than 1.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (1.5 per cent), the area of any other secondary peak is not more than 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.2 per cent) and the sum of the areas of all the secondary peaks is not more than twice the area of the principal peak in the chromatogram obtained with reference solution (b) (2.0 per cent). Ignore any peak with an area less than 0.05 times the area of the principal peak in the chromatogram obtained with reference solution (b) 0.05 per cent).

Other tests. Comply with the tests stated under Capsules.

Assay. Determine by liquid chromatography (2.4.14), as described under Related substances with following modifications.

Inject reference solution (a). The test is not valid unless the column efficiency is not less than 10000 theoretical plates, tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 2.0 per cent.

Inject reference solution (a) and the test solution.

Calculate the content of $C_{13}H_{19}N_3O_7$ in the capsules.

Storage. Store protected from moisture, at a temperature not exceeding 30°.